REMARKS

REQUEST FOR CONTINUING EXAMINATION

This Response is being filed with a Request for Continuing Examination under 37 CFR § 1.114 and the fee set forth in § 1.17(e). The Applicant, therefore, requests that the Examiner withdraw the finality of the Office Action mailed on 10 August 2006, enter the Amendments, and reconsider the application in view of the arguments presented in this Response.

CLAIMS

Claim Amendments

After entry of the present amendment, Claims 1-15, 18-28, 31, 42-44, 57, and 58 are currently pending in the application. Claims 1, 5, 19, 20, 23, 24, 25, 26, 28, 31, 43, and 44 have been amended. Claims 16 and 17 have been cancelled. Support for all claim amendments is found in the specification as filed, and there is no new matter in any of the claim amendments.

In claim 1, the recitation of specific proliferation agents has been deleted. Support for this amendment is found throughout the specification and specifically in original claim 1 in the application as filed. A concentration for transferrin has also been added to claim 1. Support for this amendment is found on page 19, lines 26-27 and on page 34, lines 17-18 of the application as filed (paragraphs [0072] and [0152] of the published application).

The term "proliferation agent" has been introduced into claim 5. This term more accurately describes the claimed invention. Support for this amendment appears throughout the application and specifically on page 14, lines 12-27 of the application as filed (paragraph [0053] of the published application).

Claims 19, 20, 23, 24, 28, 31, and 43 have been amended to make the claim language more consistent and to clarify the antecedent basis for various claim limitations. Claim 31 has also been amended to correct a typographical error. Claims 1, 25, 26, 28,

and 44 have been amended to correct the use of commas and the word "and" so the claims read more clearly.

No new matter has been introduced in any of the claim amendments.

Claim Rejections

All pending claims stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Crouch et al., *Journal of Immunological Methods*, 160: 81-88 (1993), in view of Bell et al., U.S. Patent Application Publication No. US 2002/0120098 A1, and further in view of Moore, U.S. Patent No. 5,328,844. Applicant traverses this rejection and respectfully submits that none of the cited references, either alone or in combination, render the claimed invention obvious. Applicant requests that the Examiner withdraw these rejections in view of the remarks presented herein.

As stated in the MPEP:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).
> (MPEP 706.02(j), underlining added for emphasis.)

Applicants submit that the Examiner's rejection of the pending claims is improper because the Examiner has failed to provide a clear suggestion or motivation that would have led one of ordinary skill in the art to combine or to modify the prior art references in the manner suggested by the Examiner. More importantly, even if the prior art references were combined as the Examiner suggests, the combination would not result in the claimed invention because the combined references do not teach or suggest all of the claim limitations as required for a proper 35 U.S.C. § 103(a) rejection.

The claimed invention is directed to a method for a high-throughput assay for determining the proliferative status of a population of primitive hematopoietic cells. All pending claims depend from independent claim 1.

In simple terms, the Examiner relies on (1) Crouch et al. for teaching an ATP bioluminescence assay, (2) Bell et al. for teaching various tissue culture conditions, and (3) Moore for disclosing the use of transferrin in cell growth media. The Examiner asserts that:

> It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the culture growth media composition as taught by Bell having 30% fetal bovine serum, 0.8% methyl cellulose, and in an atmosphere having between about 5% oxygen, and to include therein transferrin taught by Moore, for the culture system as taught by Crouch for maintaining cells suitable for ATP bioluminescence assay.
> (Final Office Action, mailed 10 August 2006, p.6.)

As amended, claim 1 recites:

> 1. A high-throughput assay method for rapidly determining the proliferative status of a population of primitive hematopoietic cells, the method comprising the steps of:
>
> (a) incubating a cell population comprising primitive hematopoietic cells in a cell growth medium comprising fetal bovine serum having a concentration of between 0% and about 30%, methyl cellulose having a concentration of between about 0.4% and about 0.7%, transferrin having a concentration of about 0.1 nM and in an atmosphere having between about 3.5% oxygen and about 7.5% oxygen;
>
> (b) contacting the cell population with a reagent capable of generating luminescence in the presence of ATP; and
>
> (c) detecting luminescence generated by the reagent contacting the cell population, the level of luminescence indicating the amount of ATP in the

> cell population, wherein the amount of ATP indicates the proliferative status of the primitive hematopoietic cells.

As the Examiner has acknowledged, none of the cited references teaches a cell growth medium containing methyl cellulose having a concentration of between about 0.4% and about 0.7%, as recited in claim 1. Similarly, none of cited references teaches a cell growth medium containing transferrin having a concentration of about 0.1 nM, as recited in claim 1 as amended. The Examiner relies on Moore to "disclose the beneficial effect of iron-saturated transferrin in mammalian cell growth media." (Final Office Action, mailed 10 August 2006, p.6.) The use of transferrin as disclosed by Moore is at much higher concentrations than those recited in claim 1. Moore states:

> The growth response of mammalian cells to varying amounts of transferrin indicated that the optimal range of concentration of transferrin is between approximately 1 mg/l and 10 mg/l, and is preferably 5 mg/l.
> (Moore, U.S. Patent No. 5,328,844, col. 14, lines 30-33.)

By teaching an optimal range of tranferrin for growth of mammalian cells significantly higher than the claimed concentration, Moore actually teaches against the very low concentrations of transferrin taught in the present application and recited in claim 1. Most significantly, none of the cited art is directed to a high-throughput assay method for rapidly determining the proliferative status of a population of primitive hematopoietic cells, as recited in claim 1.

Since the Examiner has failed to established a *prima facia* case of obviousness with respect to independent claim 1, all claims depending from independent claim 1 are, therefore, nonobvious. As stated in the MPEP:

> To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). ... If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). (MPEP § 2143.03, underlining added for emphasis.)

In summary, the combination of cited references would not yield the claimed invention, nor render the claimed invention obvious. For at least these reasons, Applicant respectfully requests that the Examiner withdraw the 35 U.S.C. § 103(a) rejection of the pending claims.

While the Applicant respectfully submits that the Examiner has not established a *prima facia* case of obviousness with respect to the pending claims, in order to expedite prosecution, the Applicant will be submitting additional evidence of non-obviousness in the form of an inventor's Declaration under 37 C.F.R. §1.132. As discussed with the Examiner on 12 February 2007, the Declaration will be submitted as a Supplemental Response under separate cover. The Applicant thanks the Examiner for indicating her willingness to consider the Supplemental Response when it is received.

The art of record is directed to standard tissue culture media and traditional colony forming assays. Traditional colony-forming assays measure the ability of a primitive cell to differentiate into colonies, and are, therefore, differentiation assays. The present invention is directed to a high-throughput assay method for rapidly determining the proliferative status of a population of primitive hematopoietic cells. In contrast to the colony forming assays, or differentiation assays of the past, the present invention provides a proliferation assay. None of the cited art provides the motivation, suggestion, or teaching for a high-throughput proliferation assay for primitive hematopoietic cells. The Declaration will provide additional evidence of the non-obviousness of the claimed invention.

CONCLUSION

Applicant respectfully requests that the Examiner withdraw the rejections of the pending claims based on the amendments and remarks presented herein. Applicant submits that the pending claims are patentably distinct from and over the art cited and of record, and respectfully requests the application be allowed to issuance.

Any amendments made during the prosecution of this application are intended solely to expedite prosecution of the application and are not to be interpreted as

acknowledgement of the validity of any rejection raised earlier in prosecution, nor as acknowledgement that any citation made against the application is material to the patentability of the application prior to amendment.

This Response is being filed with a Request for Continuing Examination under 37 CFR § 1.114 and the fee set forth in § 1.17(e) and with a three month extension under 37 CFR § 1.136(a). No additional fees are believed necessitated by the filing of this Response. Should any such additional fees be required, the Director is hereby authorized to deduct them from Deposit Account No. 18-2000, of which the undersigned is an authorized signatory.

As discussed with the Examiner, the undersigned attorney will contact the Examiner after filing the Supplemental Response and Declaration under 37 C.F.R. §1.132 in order to request an interview. Should the Examiner believe that there are any outstanding matters capable of resolution by a telephone interview, the Examiner is encouraged to telephone the undersigned attorney of record.

Respectfully submitted

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